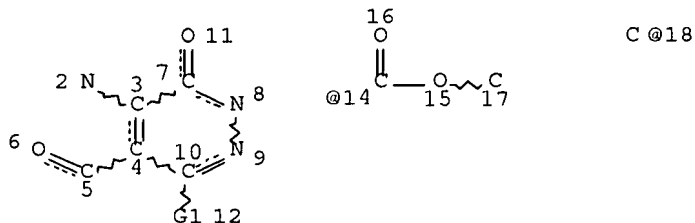


EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
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L4	1655	514/247.ccls. 514/252.01.ccls. 514/252.02.ccls. 514/252.03.ccls. 514/252.04.ccls. 514/252.05.ccls. 514/252.06.ccls.	USPAT	OR	ON	2007/09/10 12:16

=> d que l16

L9 STR



VAR G1=14/18

NODE ATTRIBUTES:

NSPEC IS R AT 18

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L11 974 SEA FILE=REGISTRY SSS FUL L9

L14 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

L16 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND (1840-2003)/PRY,AY,
PY

=> s l16 not l25

L42 5 L16 NOT L25

=> d l42 1-5 ibib ed ab hitstr hitind

L42 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:909005 HCAPLUS Full-text

DOCUMENT NUMBER: 141:81614

TITLE: Comparison of MLR, PLS and GA-MLR in QSAR analysis

AUTHOR(S): Saxena, A. K.; Prathipati, P.

CORPORATE SOURCE: Med. Chem. Div., Cent. Drug Res. Inst., Lucknow,
226001, IndiaSOURCE: SAR and QSAR in Environmental Research (
2003), 14(5-6), 433-445

CODEN: SQERED; ISSN: 1062-936X

PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 20 Nov 2003

AB The use of the internet has evolved in quant. structure-activity relationship (QSAR) over the past decade with the development of web based activities like the availability of numerous public domain software tools for descriptor calcn. and chemometric toolboxes. The importance of chemometrics in QSAR has accelerated in recent years for processing the enormous amount of information in form of predictive math. models for large datasets of mols. With the availability of huge nos. of physicochem. and structural parameters, variable selection became crucial in deriving interpretable and predictive QSAR models.

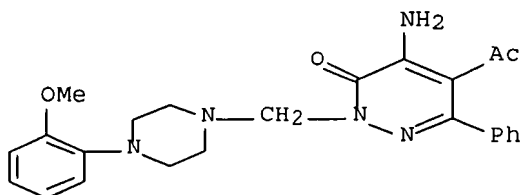
Among several approaches to address this problem, the principal component regression (PCR) and partial least squares (PLS) analyses provide highly predictive QSAR models but being more abstract, they are difficult to understand and interpret. Genetic algorithm (GA) is a stochastic method well suited to the problem of variable selection and to solve optimization problems. Consequently the hybrid approach (GA-MLR) combining GA with multiple linear regression (MLR) may be useful in derivation of highly predictive and interpretable QSAR models. In view of the above, a comparative study of stepwise-MLR, PLS and GA-MLR in deriving QSAR models for datasets of α 1-adrenoreceptor antagonists and β 3-adrenoreceptor agonists has been carried out using the public domain software Dragon for computing descriptors and free Matlab codes for data modeling.

IT 213483-34-2 213483-35-3 213483-36-4
213483-39-7

(comparison of multiple linear regression, principal component regression and genetic algorithm-multiple linear regression in QSAR anal. of adrenoreceptor agonists and antagonists)

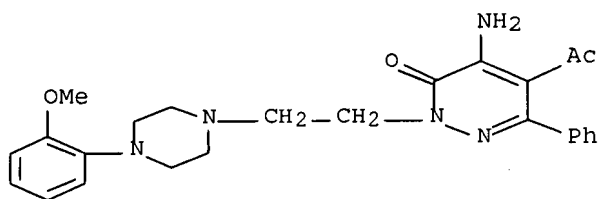
RN 213483-34-2 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[[4-(2-methoxyphenyl)-1-piperazinyl]methyl]-6-phenyl- (9CI) (CA INDEX NAME)



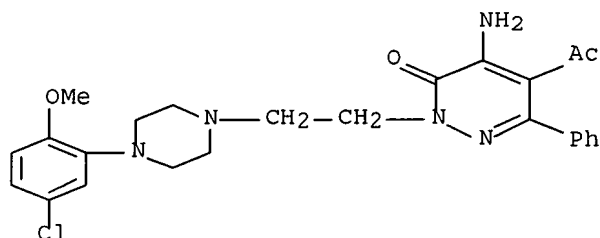
RN 213483-35-3 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)

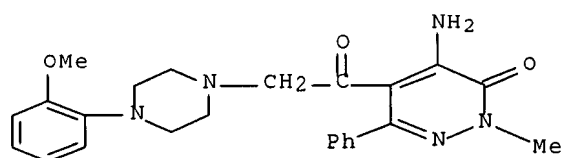


RN 213483-36-4 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



RN 213483-39-7 HCAPLUS
 CN 3(2H)-Pyridazinone, 4-amino-5-[[4-(2-methoxyphenyl)-1-piperazinyl]acetyl]-2-methyl-6-phenyl- (9CI) (CA INDEX NAME)



CC 1-1 (Pharmacology)
 IT 19216-56-9 102391-85-5 133399-66-3 134390-72-0 157396-51-5
 159182-14-6 159182-18-0 159182-21-5 159182-26-0 159182-41-9
 159182-43-1 159182-44-2 159182-45-3 159182-51-1 159182-52-2
 159182-56-6 159182-62-4 159182-77-1 159182-79-3 159182-80-6
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 192525-39-6 192525-41-0 192525-42-1 198769-20-9 209180-51-8
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 714950-98-8 714950-99-9 714951-00-5 714951-01-6 714951-02-7
 714951-03-8 714951-04-9 714951-05-0 714951-07-2 714951-08-3

(comparison of multiple linear regression, principal component regression and genetic algorithm-multiple linear regression in QSAR anal. of adrenoreceptor agonists and antagonists)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:343282 HCAPLUS Full-text

DOCUMENT NUMBER: 133:159627

TITLE: The ad hoc supermolecule approach to receptor ligand design

AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.; Cocchi, M.

CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena e Reggio Emilia, Modena, 41100, Italy

SOURCE: THEOCHEM (2000), 503(1-2), 1-16

CODEN: THEODJ; ISSN: 0166-1280

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 24 May 2000

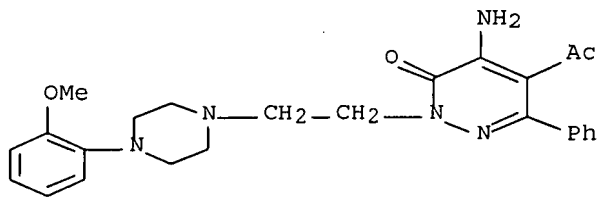
AB Among the ligand design methods based on the theor. QSAR paradigm, the simple ad hoc supermol. approach is presented and applied to a highly non-congeneric set of α 1-adrenergic receptor antagonists. The performance of the approach is satisfactory and highlights its (semi)quant. ligand design potentiality.

IT **213483-35-3 213483-36-4 213483-37-5**

(ad hoc supermol. approach to receptor ligand design)

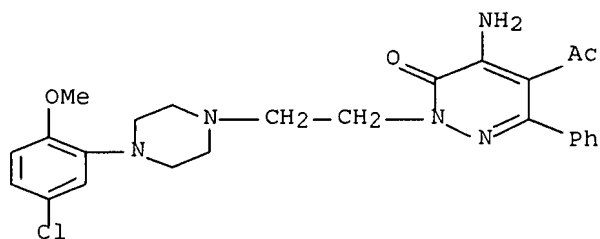
RN 213483-35-3 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



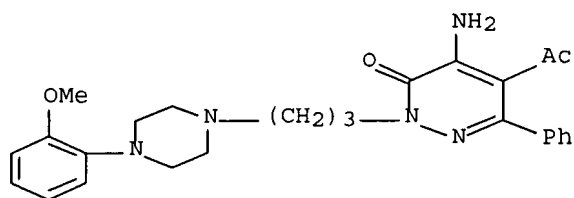
RN 213483-36-4 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]-6-phenyl- (9CI) (CA INDEX NAME)



RN 213483-37-5 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-2-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-6-phenyl- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)

Section cross-reference(s): 27, 28

IT 613-67-2 19216-56-9 67339-62-2 90402-40-7 94666-07-6
 102993-22-6 139644-60-3 151563-49-4 152735-94-9 152736-76-0
 152736-84-0 152753-37-2 169506-22-3 173059-05-7 173059-30-8
 173059-39-7 173059-46-6 173059-47-7 173059-50-2 188018-68-0
 213483-29-5 213483-30-8 213483-32-0 **213483-35-3**
213483-36-4 213483-37-5 288073-22-3 288073-23-4

(ad hoc supermol. approach to receptor ligand design)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L42 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:262337 HCAPLUS Full-text

DOCUMENT NUMBER: 126:311728

TITLE: Novel Heterocyclic-Fused Pyridazinones as Potent
 and Selective Phosphodiesterase IV Inhibitors

AUTHOR(S): Dal iaz, Vittorio; Paola Giovannoni, Maria;
 Castellana, Carla; Palacios, Jose Maria; Beleta,
 Jorge; Domenech, Teresa; Segarra, Victor

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Florence,
 50121, Italy

SOURCE: Journal of Medicinal Chemistry (1997),
 40(10), 1417-1421

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 126:311728

ED Entered STN: 24 Apr 1997

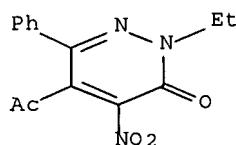
AB A series of 6-aryl-4,5-heterocyclic-fused pyridazinones were designed and synthesized as selective phosphodiesterase (PDE) IV inhibitors. Biol. evaluation of these compds. demonstrated a good selectivity profile toward the PDE III family and exhibited greatly attenuated affinity for the Rolipram high-affinity binding site that seems to be responsible for undesirable side effects. Structure-activity relationships (SARs) studies showed that the presence of an Et group at pyridazine N-2 is associated with the best potency and selectivity profile.

IT **189306-94-3P 189306-96-5P 189306-97-6P**

(intermediate; preparation of novel heterocyclic-fused pyridazinones as potent and selective phosphodiesterase IV inhibitors)

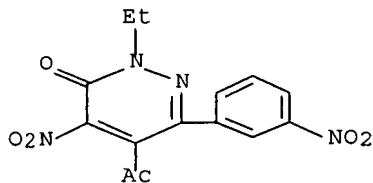
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CN 3(2H)-Pyridazinone, 5-acetyl-2-ethyl-4-nitro-6-phenyl- (9CI) (CA INDEX NAME)



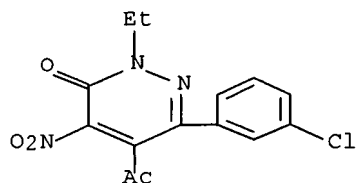
RN 189306-96-5 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-2-ethyl-4-nitro-6-(3-nitrophenyl)- (9CI) (CA INDEX NAME)



RN 189306-97-6 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-6-(3-chlorophenyl)-2-ethyl-4-nitro- (9CI) (CA INDEX NAME)



CC 1-3 (Pharmacology)

Section cross-reference(s): 28

IT 189306-87-4P 189306-88-5P 189306-89-6P 189306-90-9P
189306-91-0P 189306-92-1P 189306-93-2P **189306-94-3P**

189306-96-5P 189306-97-6P

(intermediate; preparation of novel heterocyclic-fused pyridazinones as potent and selective phosphodiesterase IV inhibitors)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1978:443310 HCAPLUS Full-text

DOCUMENT NUMBER: 89:43310

TITLE: Synthesis of pyrimido[4,5-d]pyridazin-8-one and -5-one

AUTHOR(S): Plescia, Salvatore; Dattolo, Gaetano; Sprio, Vincenzo

CORPORATE SOURCE: Italy

SOURCE: Atti della Accademia di Scienze, Lettere e Arti di Palermo, Parte 1: Scienze (1976), 34(2), 377-80

CODEN: AASLAN; ISSN: 0365-0448

DOCUMENT TYPE: Journal

LANGUAGE: Italian

ED Entered STN: 12 May 1984

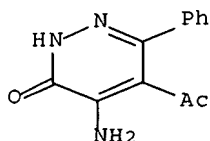
AB Pyrimidopyridazinones I (R = Me, Ph, R1R2 = CMe:NCH:N) were obtained in 80-5% yield by cyclocondensation of I (R1 = Ac, R2 = NH2) with HCONH2. Reaction of I (R = Ph, R1 = NH2, R2 = Ac) with HCONH2 similarly gave I (R = Ph, R1R2 = N:CHN:CMe).

IT 17335-08-9

(cyclocondensation of, with formamide)

RN 17335-08-9 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-6-phenyl- (8CI, 9CI) (CA INDEX NAME)



CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

IT 17334-69-9 17335-04-5 17335-08-9

(cyclocondensation of, with formamide)

L42 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1968:49558 HCAPLUS Full-text

DOCUMENT NUMBER: 68:49558

TITLE: Nitrogen heterocycles. II. Hydrogenation of isoxazolo[3,4-d]pyridazin-7-ones, isoxazolo[3,4-d]pyridazin-4-ones, and isoxazolo[3,4-d]pyridazine-4,7-diones

AUTHOR(S): Sprio, Vincenzo; Ajello, Enrico; Mazza, Acursio

CORPORATE SOURCE: Univ. Cagliari, Cagliari, Italy

SOURCE: Annali di Chimica (Rome, Italy) (1967), 57(7), 836-45

CODEN: ANCRAI; ISSN: 0003-4592

DOCUMENT TYPE: Journal

LANGUAGE: Italian

ED Entered STN: 12 May 1984

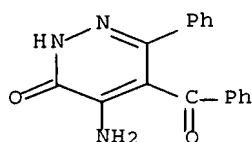
AB Hydrogenation of the title compds. gives 4-amino-5-acylpyridazine-3-ones, 4-amino-5-acylpyridazine-3,6-diones, and 5-amino-4-acylpyridazin-3-ones. Thus, a cold solution of 0.01 mole of I, II, or III in 200 ml. EtOH was hydrogenated over Raney nickel in a Parr apparatus for 12 hrs. Filtration and concentration of the solution gives the products (IV-VI). Prepared were the following IV (R1, R2, and m.p. given): Me, Me, 234° (EtOH) [diacetyl derivative m. 202° (EtOH); oxime m. 249° (EtOH)]; Ph, Ph, 229-30° (EtOH) [acetyl derivative m. 197° (EtOH)]; Ph, Me, 201-3° (EtOH) [acetyl derivative m. 237° (EtOH)]. V decomposed 338°; VI m. 302° (EtOH) [oxime m. 242° (EtOH)]. Ir and N.M.R. spectra are given.

IT 17335-02-3P 17335-08-9P 19027-16-8P
19027-17-9P

(preparation of)

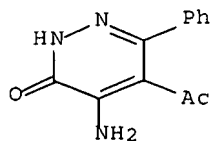
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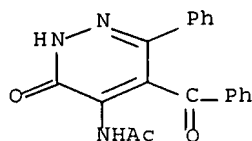
RN 17335-08-9 HCAPLUS

CN 3(2H)-Pyridazinone, 5-acetyl-4-amino-6-phenyl- (8CI, 9CI) (CA INDEX NAME)



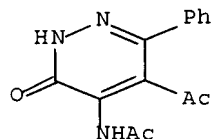
RN 19027-16-8 HCAPLUS

CN Acetamide, N-(5-benzoyl-2,3-dihydro-3-oxo-6-phenyl-4-pyridazinyl)- (8CI) (CA INDEX NAME)



RN 19027-17-9 HCAPLUS

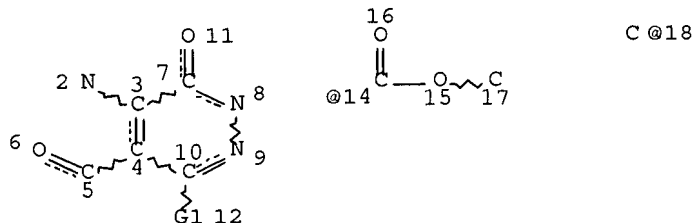
CN Acetamide, N-(5-acetyl-2,3-dihydro-3-oxo-6-phenyl-4-pyridazinyl)- (8CI) (CA INDEX NAME)



CC 28 (Heterocyclic Compounds (More Than One Hetero Atom))
 IT 17334-64-4P 17334-65-5P 17334-66-6P 17334-67-7P 17334-68-8P
 17334-69-9P 17334-70-2P **17335-02-3P** 17335-03-4P
 17335-04-5P 17335-05-6P 17335-06-7P **17335-08-9P**
19027-16-8P 19027-17-9P 19027-46-4P
 (preparation of)

=> d que 125

L9 STR



VAR G1=14/18
 NODE ATTRIBUTES:
 NSPEC IS R AT 18
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

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 L14 37 SEA FILE=HCAPLUS ABB=ON PLU=ON L11
 L18 77 SEA FILE=HCAPLUS ABB=ON PLU=ON DAL PIAZ, V?/AU
 L19 4 SEA FILE=HCAPLUS ABB=ON PLU=ON AGUILAR IZQUIERDO, N?/AU
 L20 9 SEA FILE=HCAPLUS ABB=ON PLU=ON BUIL ALBERO MARIA, A?/AU
 L21 2 SEA FILE=HCAPLUS ABB=ON PLU=ON CARRASCAL RIERA, M?/AU
 L22 10 SEA FILE=HCAPLUS ABB=ON PLU=ON GRACIA FERRER, J?/AU
 L23 41 SEA FILE=HCAPLUS ABB=ON PLU=ON GIOVANNONI, M?/AU
 L24 15 SEA FILE=HCAPLUS ABB=ON PLU=ON VERGELLI, C?/AU
 L25 27 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND ((L18 OR L19 OR
 L20 OR L21 OR L22 OR L23 OR L24))

=> d que 141

L32 0 SEA AGUILAR IZQUIERDO, N?/AU
 L33 2 SEA BUIL ALBERO MARIA, A?/AU

10/539,821

L34 0 SEA CARRASCAL RIERA, M?/AU
L35 2 SEA GRACIA FERRER, J?/AU
L36 113 SEA GIOVANNONI, M?/AU
L37 26 SEA VERGELLI, C?/AU
L38 35 SEA (L32 OR L33 OR L34 OR L35 OR L36 OR L37) AND (PYRIDAZIN
? AND INHIBITORS?)
L39 117 SEA DAL PIAZ, V?/AU
L40 35 SEA L39 AND (PYRIDAZIN? AND INHIBITORS?)
L41 39 SEA L38 OR L40

=> dup rem l25 l41

FILE 'HCAPLUS' ENTERED AT 11:19:51 ON 15 DEC 2006
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FILE 'MEDLINE' ENTERED AT 11:19:51 ON 15 DEC 2006
PROCESSING COMPLETED FOR L25
PROCESSING COMPLETED FOR L41

L43 38 DUP REM L25 L41 (28 DUPLICATES REMOVED)
ANSWERS '1-27' FROM FILE HCAPLUS
ANSWERS '28-34' FROM FILE EMBASE
ANSWER '35' FROM FILE BIOSIS
ANSWERS '36-38' FROM FILE MEDLINE

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L43 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2002:815783 HCAPLUS Full-text
DOCUMENT NUMBER: 138:378543
TITLE: Synthesis and evaluation of some
pyrazolo[3,4-d]pyridazinones and analogues as PDE
5 inhibitors potentially useful as peripheral
vasodilator agents
AUTHOR(S): **Dal Piaz, Vittorio**; Castellana, Maria
Carla; **Vergelli, Claudia**;
Giovannoni, Maria Paola; Gavalda, Amadeu;
Segarra, Victor; Beleta, Jorge; Ryder, Hamish;
Palacios, Jose Maria
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Florence,
50121, Italy
SOURCE: Journal of Enzyme Inhibition and Medicinal
Chemistry (2002), 17(4), 227-233
CODEN: JEIMAZ; ISSN: 1475-6366
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:378543
AB A series of pyrazolo[3,4-d]pyridazinones and analogs, potentially useful as
peripheral vasodilators, were synthesized and evaluated as inhibitors of PDE5
extracted from human platelets. Several of them showed IC50 values in the
range 0.14-1.4 µM. A good activity and selectivity profile vs. PDE6 was found
for compound (6-benzyl-3-methyl-1- isopropyl-4-phenylpyrazolo[3,4-d]

pyridazin-7(6H)-one). Structure-activity relationship studies demonstrated the essential role played by the benzyl group at position-6 of the pyrazolopyridazine system. Other types of pyridazinones fused with five and six membered heterocycles (pyrrole, isoxazole, pyridine and dihydropyridine), as well as some open models were prepared and evaluated. Besides the pyrazole, the best fused systems proved to be isoxazole and pyridine.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 2002:154884 HCAPLUS Full-text

DOCUMENT NUMBER: 137:362487

TITLE: Isoxazolo[3,4-d]pyridazinones and analogues as Leishmania mexicana PDE inhibitors

AUTHOR(S): Dal Piaz, Vittorio; Rascon, A.; Dubra, M. E.; Giovannoni, M. P.; Vergelli, C.; Castellana, M. C.

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universite Firenze, Florence, 50121, Italy

SOURCE: Farmaco (2002), 57(2), 89-96

CODEN: FRMCE8; ISSN: 0014-827X

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of isoxazolopyridazinones and analogs has been prepared and evaluated as Leishmania mexicana phosphodiesterase (PDE) inhibitors. Some of the synthesized compds. showed a moderate PDE inhibitory activity at 100 μ M and preliminary structure-activity relationships were discussed.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 1999:304425 HCAPLUS Full-text

DOCUMENT NUMBER: 130:352238

TITLE: Isoxazolo-[3,4-d]-pyridazin-7-(6H)-one as a potential substrate for new aldose reductase inhibitors

AUTHOR(S): Costantino, Luca; Rastelli, Giulio; Gamberini, M. Cristina; Giovannoni, M. Paola; Dal Piaz, Vittorio; Vianello, Paola; Barlocco, Daniela

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Via G. Campi 183, Modena, 41100, Italy

SOURCE: Journal of Medicinal Chemistry (1999), 42(11), 1894-1900

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The isoxazolo[3,4-d]pyridazin-7(6H)-one I (R = Ph, Me, 4-ClC₆H₄, etc.) and its corresponding open derivs. 5-acetyl-4-amino(4-nitro)-6- substituted-3(2H)-pyridazinones II (X = NH₂, NO₂) were used as simplified substrates for the synthesis of new aldose reductase inhibitors with respect to the previously reported 5,6-dihydrobenzo[h]cinnolin-3(2H)-one-2 acetic acid III. Moreover, a few derivs. lacking the 5-acetyl group were prepared Several compds. derived from I displayed inhibitory properties comparable to those of Sorbinil. In this class the presence at position 6 of a Ph carrying an electron-withdrawing substituent proved to be beneficial, independently from its position on the

ring I [R = 4-ClC₆H₄, 2-, 3-, 4-O₂NC₆H₄, R' = (CH₂)_nCO₂H, n = 1]. Acetic acid derivs. were more effective than propionic and butyric analogs. On the contrary, all the monocyclic compds. IV (R = Ph, Me, n = 1-3), V (R = Ph, CH₂Ph, 4-ClC₆H₄, etc.), and VI (R = H, CH₂Ph, CH₂CH₂Ph, CH₂CH₂-pyrid-2-yl) were either inactive or only weakly active. The 3-methyl-4-(p-chlorophenyl)isoxazolo[3,4-d]pyridazin-7(6H)-one acetic acid, which proved to be the most potent derivative, was also investigated in mol. modeling studies, to assess possible similarities in its interaction with the enzyme, with respect to the model III.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1998:793835 HCAPLUS Full-text

DOCUMENT NUMBER: 130:162741

TITLE: Heterocyclic-fused 3(2H)-pyridazinones as potent and selective PDE IV inhibitors: further structure-activity relationships and molecular modeling studies

AUTHOR(S): **Dal Piaz, Vittorio**; Paola Giovannoni, Maria; Castellana, Carla; Palacios, Jose Maria; Beleta, Jorge; Domenech, Teresa; Segarra, Victor

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Florence, 50121, Italy

SOURCE: European Journal of Medicinal Chemistry (1998), 33(10), 789-797

CODEN: EJMCA5; ISSN: 0223-5234

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A novel group of heterocyclic-fused 3(2H)-pyridazinones were synthesized and evaluated as PDE III and PDE IV inhibitors and their affinity for 3H Rolipram high affinity binding site was determined. The obtained data demonstrated that some of the new compds. are endowed with potent and selective PDE IV inhibitory activity and greatly attenuated affinity for the Rolipram high affinity binding site that seems to be responsible for unwanted effects. Theor. calcns., performed on representative compds., demonstrated the presence of three hydrogen-bonding acceptor regions, of which one looks quite different with respect to literature compds. This finding could explain the different pharmacol. profile of the title compds. with respect to the analogs reported in the literature.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 1997:508095 HCAPLUS Full-text

DOCUMENT NUMBER: 127:214587

TITLE: Synthesis of 4,5-functionalized-2-methyl-6-(substituted aryl)-3(2H)-pyridazinones: a new group of potent platelet aggregation inhibitors

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Giovannoni, Maria Paola

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy

SOURCE: Farmaco (1997), 52(3), 173-178

CODEN: FRMCE8; ISSN: 0014-827X

PUBLISHER: Societa Chimica Italiana

DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 127:214587
 AB A series of 4,5-functionalized-2-methyl-6-(substituted phenyl)-3(2H)-pyridazinones were synthesized and evaluated as platelet aggregation inhibitors in human platelet rich plasma (PRP). The new products generally displayed significant higher activity with respect to the corresponding unsubstituted aryl compds. Several compds. appeared to be of particular interest with IC50s in the submicromolar range. Structure-activity relationships (SARs) are discussed.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 1996:732957 HCAPLUS Full-text

DOCUMENT NUMBER: 126:84307

TITLE: Synthesis and evaluation as platelet aggregation inhibitors of 6-phenyl-2,4-substituted-3(2H)-pyridazinones and their rigid analogs benzo[h]cinnolin-3,5-diones

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**; Franconi, Flavia

CORPORATE SOURCE: Dip. Scienze Farmaceutiche, Univ. Firenze, 50121, Italy

SOURCE: Drug Design and Discovery (1996), 14(1), 53-75
 CODEN: DDDIEV; ISSN: 1055-9612

PUBLISHER: Harwood

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 5-acyl-6-phenyl-2,4-substituted-3(2H)-pyridazinones and analogous benzo[h]cinnolin-3,5-diones with reduced flexibility has been prepared and evaluated as human platelet aggregation inhibitors. The 4-methylsulfoxide I was the most potent compound of the series (IC50 = 1.2 μ M). SAR studies have shown the primary importance of an electroneg. substituent at position 4 and an acetyl group at position 5 of the pyridazine system for potent platelet aggregation inhibitory activity. Biol. tests performed on a group of representative compds. showed that these products have no effects on prostaglandins, thromboxanes, and nitric oxide biosynthetic pathways. Some of synthesized compds. produced a moderate increase of cAMP level in platelets which does not depend on adenylate cyclase stimulation. Tests performed on human platelet phosphodiesterase III have shown that these compds. are not inhibitors of this enzyme.

L43 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 1994:645151 HCAPLUS Full-text

DOCUMENT NUMBER: 121:245151

TITLE: 4-substituted-5-acetyl-2-methyl-6-phenyl-3(2H)pyridazinones as PGE2 and IL-1 release inhibitors from mouse adherent macrophages

AUTHOR(S): **Dal Piaz, V.**; **Giovannoni, M. P.**; Ciciani, G.; Becherucci, C.; Parente, L.

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy

SOURCE: Pharmacological Research (1994), 29(4), 367-72
 CODEN: PHMREP; ISSN: 1043-6618

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of 4,5-functionalized 3(2H)-pyridazinones (I, R = NO2, NH2, Br, SOME) were evaluated as PGE2 and interleukin-1 (IL-1) release inhibitors from mouse

adherent macrophages. Among the tested compds. only I (R = NH₂) was devoid of activity in both the PGE₂ and IL-1 tests, whereas the other compds., showed a significant dose-dependent activity. I (R = NO₂, Br or SOMe) inhibited PGE₂ better than IL-1 release from stimulated macrophages. I (R = SOMe), which showed an IC₅₀=5.5 µM in the IL-1 test, appears to be a promising agent in this cell inflammation model. Structure-activity relation studies demonstrated the importance of the presence of a substituent characterized by a pos. σ constant at position 4 of the pyridazine system.

L43 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 1991:441291 HCAPLUS Full-text

DOCUMENT NUMBER: 115:41291

TITLE: 5-Acyl-6-aryl-4-nitro-3(2H)pyridazinones and related 4-amino compounds: synthesis and pharmacological evaluation

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Turco, Giovanni; **Giovannoni, Maria Paola**; Miceli, Mauro; Pirisino, Renato; Perretti, Mauro
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121, Italy

SOURCE: Journal of Pharmaceutical Sciences (1991), 80(4), 341-8

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several 4-nitro- and 4-amino-5-acyl-6-acyl-3(2H)-pyridazinones were prepared and their in vitro and ex vivo antiaggregatory properties were evaluated. 4-Nitro derivs. generally showed good activity in vitro towards arachidonic acid (AA)-induced human blood platelet aggregation. The 4-amino compound (I, R₁ = R₃ = Me; R₂ = Ph; R₄ = NH₂) which has weak in vitro activity, exhibited antiplatelet activity, particularly on adenosine diphosphate (ADP)-induced aggregation ex vivo in rabbit. Moreover, the same compound was active in platelet-activating factors (PAF)-induced rat paw hyperalgesia and to be endowed with low acute oral toxicity. The 4-amino derivs. and the other pyridazinones administered orally to rats were also more potent anti-inflammatory agents than acetylsalicylic acid. I (R₁ = R₃ = Me; R₂ = Ph; R₄ = NO₂ or NH₂) tested in vitro on lipopolysaccharide (LPS)-stimulated rat peritoneal macrophages, were active in the inhibition of prostaglandin E₂ (PGE₂) production and interleukin-1 activity. Structure-activity relation studies in the series of antiaggregating pyridazinones showed the primary importance of the nitro and acetyl substituents at positions 4 and 5, resp. Hydrophobic substituents at position 2 were also required for better activity.

L43 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1354871 HCAPLUS Full-text

DOCUMENT NUMBER: 144:88299

TITLE: Preparation of pyridazin-3(2H)-one derivatives as PDE4 inhibitors for the treatment of pathological diseases

INVENTOR(S): **Aguilar Izquierdo, Nuria**; **Carrascal Riera, Marta**; **Dal Piaz, Vittorio**; **Gracia Ferrer, Jordi**; Lumeras Amador, Wenceslao; Masdeu Margalef, Maria del Carmen; Warrellow, Graham

PATENT ASSIGNEE(S): Almirall Prodesfarma, S.A., Spain

SOURCE: PCT Int. Appl., 173 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005123693	A1	20051229	WO 2005-EP6712	20050621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2251867	A1	20060501	ES 2004-1512	20040621
PRIORITY APPLN. INFO.:			ES 2004-1512	A 20040621

OTHER SOURCE(S): MARPAT 144:88299

AB The invention relates to new therapeutically useful pyridazin-3(2H)-one derivs. I [wherein R1 = H or (un)substituted alk(en/yn)yl; R2 = (un)substituted heteroaryl; R3 = H, alkyl aryl, etc., R4 = (un)substituted (hetero)aryl, and pharmaceutically acceptable salts or N-oxides thereof], to their preps., and to pharmaceutical compns. containing them. These compds. are potent inhibitors of phosphodiesterase 4 (PDE4), and are thus useful in the treatment, prevention or suppression of pathol. conditions, diseases and disorders known to be susceptible of being improved by inhibition of PDE4, such as asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease. For example, II, which had an IC50 of 0.07 nM in the PDE4 inhibition assay, was synthesized by esterification of the corresponding acid (preparation given) with chloromethyl pivalate.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1350734 HCAPLUS Full-text
 DOCUMENT NUMBER: 144:88298
 TITLE: Preparation of pyridazin-3(2H)-one derivatives as PDE4 inhibitors for the treatment of pathological diseases
 INVENTOR(S): **Buil Albero, Maria Antonia; Dal Piaz, Vittorio;** Garrido Rubio, Yolanda;
Gracia Ferrer, Jordi; Pages Santacana, Lluís Miquel; Taltavull Moll, Joan
 PATENT ASSIGNEE(S): Almirall Prodesfarma, SA, Spain
 SOURCE: PCT Int. Appl., 104 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005123692 A1 20051229 WO 2005-EP6304 20050613
WO 2005123692 C1 20060504
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN,
MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU,
SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA,
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC,
NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG
ES 2251866 A1 20060501 ES 2004-1500 20040618
PRIORITY APPLN. INFO.: ES 2004-1500 A 20040618

OTHER SOURCE(S): MARPAT 144:88298

AB The invention relates to new therapeutically useful pyridazin-3(2H)-one
derivs. I [wherein R1 = H or (un)substituted alk(en/yn)yl; R2 =
(un)substituted heteroaryl; R3 = H or alkylcarbonyl; R4 = H, alkyl, aryl,
etc., and pharmaceutically acceptable salts or N-oxides thereof], to their
preps., and to pharmaceutical compns. containing them. These compds. are
potent inhibitors of phosphodiesterase 4 (PDE4), and are thus useful in the
treatment, prevention or suppression of pathol. conditions, diseases and
disorders known to be susceptible of being improved by inhibition of PDE4,
such as asthma, chronic obstructive pulmonary disease, rheumatoid arthritis,
atopic dermatitis, psoriasis and irritable bowel disease. For example, II,
which had an IC50 of 0.36 nM in the PDE4 inhibition assay, was synthesized by
esterification of the corresponding acid (preparation given) with chloromethyl
2,2-dimethylbutyrate.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L43 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:472131 HCAPLUS Full-text

DOCUMENT NUMBER: 143:26620

TITLE: Preparation of pyridazin-3(2H)-ones and their use
as PDE4 inhibitors

INVENTOR(S): **Dal Piaz, Vittorio; Aguilar
Izquierdo, Nuria; Buil Albero, Maria
Antonia; Garrido Rubio, Yolanda;
Giovannoni Maria, Paola; Gracia
Ferrer, Jordi; Lumeras Amador, Wenceslao;
Vergelli, Claudia**

PATENT ASSIGNEE(S): Almirall Prodesfarma, S. A., Spain

SOURCE: PCT Int. Appl., 132 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
WO 2005049581	A1	20050602	WO 2004-EP12604	20041108
WO 2005049581	C1	20060504		
W:				

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

10/539,821

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
 MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
 SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
 VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
 AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
 DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL,
 PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
 GQ, GW, ML, MR, NE, SN, TD, TG
 ES 2232306 A1 20050516 ES 2003-2613 20031110
 ES 2232306 B1 20060801
 AU 2004291282 A1 20050602 AU 2004-291282 20041108
 CA 2545193 AA 20050602 CA 2004-2545193 20041108
 EP 1682519 A1 20060726 EP 2004-797700 20041108
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
 PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU,
 PL, SK, HR, IS
 CN 1878759 A 20061213 CN 2004-80033113 20041108
 NO 2006002726 A 20060612 NO 2006-2726 20060612
 PRIORITY APPLN. INFO.: ES 2003-2613 A 20031110
 WO 2004-EP12604 W 20041108

OTHER SOURCE(S): MARPAT 143:26620

AB Title compds. I [R1-2 = H, acyl, alkoxycarbonyl, etc.; R3 = mono/polycyclic
 (hetero)aryl, etc.; R4 = H, OH, alkoxy, amino, etc.; R5 = carboxy,
 mono/polycyclic (hetero)aryl, etc.] are prepared For instance, 1-Ethyl-3-(4-
 fluorophenyl)-6-oxo-5-((pyridin-3-yl)amino)-1,6- dihydropyridazine-4-
 carbonitrile (II) is prepared from 5-Amino-1-ethyl-3-(4-fluorophenyl)-6-oxo-
 1,6-dihydropyridazine-4- carbonitrile (preparation given) and 3-bromopyridine.
 II has IC50 = 5.4 for PDE4. I are useful for the treatment of asthma, COPD,
 etc.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L43 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:565225 HCAPLUS Full-text

DOCUMENT NUMBER: 141:106481

TITLE: Preparation of pyridazin-3(2H)-ones as
 Phosphodiesterase 4 (PDE4) inhibitors

INVENTOR(S): **Dal Piaz, Vittorio; Aguilar
 Izquierdo, Nuria; Buil Albero Maria,
 Antonia; Carrascal Riera, Marta;
 Gracia Ferrer, Jordi; Giovannoni,
 Maria Paola; Vergelli, Claudia**

PATENT ASSIGNEE(S): Almirall Prodesfarma Sa, Spain

SOURCE: PCT Int. Appl., 212 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058729	A1	20040715	WO 2003-EP14722	20031222
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,			
	CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,			

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
 MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
 SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
 VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
 DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
 SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

ES 2211344	A1	20040701	ES 2002-3003	20021226
ES 2211344	B1	20051001		
CA 2512099	AA	20040715	CA 2003-2512099	20031222
AU 2003290110	A1	20040722	AU 2003-290110	20031222
EP 1575926	A1	20050921	EP 2003-782471	20031222

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
 PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

BR 2003016883	A	20051025	BR 2003-16883	20031222
CN 1753876	A	20060329	CN 2003-80109897	20031222
JP 2006515302	T2	20060525	JP 2004-562819	20031222
NO 2005003614	A	20050926	NO 2005-3614	20050725
US 2006173008	A1	20060803	US 2005-539821	20051214

PRIORITY APPLN. INFO.:

ES 2002-3003 A 20021226

WO 2003-EP14722 W 20031222

OTHER SOURCE(S): MARPAT 141:106481

AB Title compds. I [wherein R1, R2 = independently H, acyl, hydroxycarbonyl, alkoxy carbonyl, monoalkyl/dialkyl/carbamoyl, (un)substituted alk(en/yn)yl, hetero/aryl, (un)saturated heterocyclyl, etc.; R3 = (un)substituted monocyclic or polycyclic hetero/aryl; R5 = (un)substituted alkoxy carbonyl, monocyclic or polycyclic hetero/aryl; R4 = H, OH and derivs., NH2 and derivs., (un)substituted alk(en/yn)yl, etc.; and their N-oxides and pharmaceutically acceptable salts] were prepared as potent and selective inhibitors of Phosphodiesterase 4 (PDE4). Four pharmaceutical compns. are given. For example, II was prepared by hydrogenation of 5-acetyl-4-amino-2-ethyl-6-(pyridin-3-yl)pyridazin-3(2H)-one over Pd/C in ethanol, and reaction of the amine with 3-fluorophenylboronic acid in the presence of Cu(OAc)2/TEA/mol. sieves/CH2Cl2. Preferred I exhibited an IC50 value < 30 nM for the inhibition of PDE4. I and their pharmaceutical compns. are useful for prevention and treatment of asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease (no data).

L43 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:931340 HCAPLUS Full-text

DOCUMENT NUMBER: 140:5060

TITLE: Preparation of pyridazin-3(2H)-ones as
 Phosphodiesterase 4 (PDE4) inhibitors

INVENTOR(S): Dal Piaz, Vittorio; Giovannoni,
 Maria Paola; Vergelli, Claudia;
 Aguilar, Izquierdo Nuria

PATENT ASSIGNEE(S): Almirall Prodesfarma Sa, Spain; Aguilar Izquierdo,
 Nuria

SOURCE: PCT Int. Appl., 145 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003097613	A1	20031127	WO 2003-EP5056	20030514
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2195785	A1	20031201	ES 2002-1111	20020516
ES 2195785	B1	20050316		
CA 2485896	AA	20031127	CA 2003-2485896	20030514
AU 2003236648	A1	20031202	AU 2003-236648	20030514
EP 1503992	A1	20050209	EP 2003-735387	20030514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003010106	A	20050222	BR 2003-10106	20030514
JP 2005533024	T2	20051104	JP 2004-505346	20030514
NZ 536604	A	20060728	NZ 2003-536604	20030514
ZA 2004009173	A	20050729	ZA 2004-9173	20041111
NO 2004005461	A	20050119	NO 2004-5461	20041215
US 2006052379	A1	20060309	US 2005-513219	20050629
PRIORITY APPLN. INFO.:			ES 2002-1111	A 20020516
			WO 2003-EP5056	W 20030514

OTHER SOURCE(S): MARPAT 140:5060

AB Title compds. I [wherein R1 = H, acyl, alkoxycarbonyl, monoalkyl/dialkyl/carbamoyl, (un)substituted alkyl, (CH2)n-R6; n = 0 to 4; R6 = cycloalkyl, (un)substituted aryl, 3- to 7-membered heterocyclyl; R2 = R1, (un)substituted alkyl; R3, R5 = independently (un)substituted monocyclic or bicyclic aryl; R4 = H, OH and derivs., NH2 and derivs., (un)substituted alkyl, (CH2)n-R6; with the proviso that when R2 = H and R3, R4 = unsubstituted Ph, R1 is not methyl; and their pharmaceutical acceptable salts] were prepared as potent and selective inhibitors of Phosphodiesterase 4 (PDE4). Four pharmaceutical compns. are given. For example, II was prepared by hydrogenation of 6-ethyl-3-methyl-4-phenylisoxazolo[3,4-d]pyridazin-7(6H)-one over Pd/C in ethanol, and reaction of the resulting 4-aminopyridazinone with 3-fluorophenylboronic acid in the presence of Cu(OAc)2/TEA/mol. sieves/CH2Cl2. Selected I exhibited an IC50 value < 20 nM for the inhibition of PDE4. I and their pharmaceutical compns. are useful for prevention and treatment of asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, atopic dermatitis, psoriasis and irritable bowel disease (no data).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:829129 HCAPLUS Full-text
 DOCUMENT NUMBER: 140:357279
 TITLE: 4-Amino-3(2H)-pyridazinones bearing arylpiperazinylalkyl groups and related compounds: synthesis and antinociceptive activity
 AUTHOR(S): Dal Piaz, Vittorio; Vergelli,

Claudia; Giovannoni, Maria Paola;

Scheideler, Mark A.; Petrone, Giuseppe; Zaratin, Paola

CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Università di Firenze, Florence, 50121, Italy

SOURCE: Farmaco (2003), 58(11), 1063-1071

CODEN: FRMCE8; ISSN: 0014-827X

PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:357279

AB A series of 4-amino-3(2H)-pyridazinones substituted at position 2 with arylpiperazinylalkyl groups and analogs were synthesized and their antinociceptive effect was evaluated in the mouse abdominal constriction model. Preliminary SARs studies were performed. Several of the novel compds. dosed at 100 mg/kg s.c. significantly reduced the number of writhes induced by the noxious stimulus. Compound I showed 100% inhibition of writhes and was able to protect all the treated animals from the effect of the chemical stimulus. Subsequent dose-response studies revealed I to be almost 40-fold more potent than the structurally related Emorfazone.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:435617 HCAPLUS Full-text

DOCUMENT NUMBER: 135:180739

TITLE: Phenylpiperazinylalkylamino Substituted Pyridazinones as Potent $\alpha 1$ Adrenoceptor Antagonists

AUTHOR(S): Barlocco, Daniela; Cignarella, Giorgio; Dal Pia, Vittorio; Giovannoni, M. Paola; De Benedetti, Pier G.; Fanelli, Francesca; Montesano, Federica; Poggesi, Elena; Leonardi, Amedeo

CORPORATE SOURCE: Istituto Chimico Farmaceutico e Tossicologico, Milan, 20131, Italy

SOURCE: Journal of Medicinal Chemistry (2001), 44(15), 2403-2410

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB QSAR models have been used for designing a series of compds. characterized by a N-phenylpiperazinylalkylamino moiety linked to substituted pyridazinones, which have been synthesized. Measurements of the binding affinities of the new compds. toward the $\alpha 1a$ -, $\alpha 1b$ -, and $\alpha 1d$ -AR cloned subtypes as well as the 5-HT_{1A} receptor have been done validating, at least in part, the estns. of the theor. models. This study provides insight into the structure activity relationships of the $\alpha 1$ -ARs ligands and their $\alpha 1$ -AR/5-HT_{1A} selectivity.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:566668 HCAPLUS Full-text

DOCUMENT NUMBER: 131:286474

TITLE: New synthesis of differently fused pyridazinoquinolines

AUTHOR(S): **Dal Piaz, Vittorio; Giovannoni, Maria Paola; Ciciani, Giovanna; Vergelli, Claudia**

CORPORATE SOURCE: Dipartimento Scienze Farmaceutiche, Univ. Firenze, Florence, I-50121, Italy

SOURCE: Synlett (1999), (9), 1453-1455
CODEN: SYNLES; ISSN: 0936-5214

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:286474

AB Treatment of 4-chloro- and 4-(methylthio)-5-acetyl-2-methyl-6-(2-nitrophenyl)-3(2H)-pyridazinone with SnCl₂/HCl afforded pyridazino[4,3-c]quinolinones, whereas a pyridazino[4,5-b]quinolinone was prepared by reduction of 5-acetyl-4-anilino-6-phenyl-3(2H)-pyridazinone with NaBH₄, followed by dehydration with polyphosphoric acid.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:542409 HCAPLUS Full-text

DOCUMENT NUMBER: 129:260414

TITLE: Isoxazolo[3,4-d]pyridazin-7(6H)-ones and their corresponding 4,5-disubstituted-3-(2H)-pyridazinone analogs as new substrates for α 1-adrenoceptor selective antagonists: synthesis, modeling, and binding studies

AUTHOR(S): Montesano, Federica; Barlocco, Daniela; **Dal Piaz, Vittorio**; Leonardi, Amedeo; Poggesi, Elena; Fanelli, Francesca; De Benedetti, Piero G.

CORPORATE SOURCE: 1st. Chimica Farmaceutica e Tossicologica, Milan, 20131, Italy

SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(7), 925-935

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of phenylpiperazinylalkyl moieties were attached to monocyclic or bicyclic substituted pyridazinones and the new compds. tested for their affinity towards α 1-adrenoceptor and its α 1a, α 1b and α 1d subtypes, as well as serotonin 5-HT_{1A} receptor. Several analogs showed remarkable potency and selectivity towards α 1a, and α 1d with respect to α 1b subtype. None of the test compds. exhibited significant affinity for 5-HT_{1A} receptor. Finally, on the basis of the α 1-AR subtypes 3D models recently proposed, we have elaborated theor. interaction models for the new compds. The theor. study allowed us to predict the affinity of the new compds. as well as to infer the structural/dynamics determinants of their interaction with the three α 1-AR subtypes.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:137308 HCAPLUS Full-text

DOCUMENT NUMBER: 124:289447

TITLE: 4,5-Functionalized 6-phenyl-3(2H)-pyridazinones: synthesis and evaluation of antinociceptive

activity
 AUTHOR(S): **Dal Piaz, V.; Giovannoni, M. P.**
 ; Ciciani, G.; Barlocco, D.; Giardina, G.;
 Petrone, G.; Clarke, G. D.
 CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121,
 Italy
 SOURCE: European Journal of Medicinal Chemistry (1996),
 31(1), 65-70
 CODEN: EJMCA5; ISSN: 0223-5234
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB 2-Substituted 4,5-functionalized 6-phenyl-3(2H)-pyridazinones were synthesized
 and their antinociceptive activities were evaluated in the mouse abdominal
 constriction model. Single dose studies showed that compds. I and II were
 more active than the reference drug, Emorfazone, in inhibiting the effects of
 the noxious chemical stimulus, p-phenylquinone. Subsequent dose-response
 studies revealed I to be almost seven-fold more potent than Emorfazone.

L43 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:534061 HCAPLUS Full-text
 DOCUMENT NUMBER: 121:134061
 TITLE: 5-Acetyl-2-methyl-4-nitro-6-phenyl-3(2H)-
 pyridazinone: versatile precursor to
 hetero-condensed pyridazinones

AUTHOR(S): **Dal Piaz, V.; Ciciani, G.;**
Giovannoni, M. P.
 CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121,
 Italy
 SOURCE: Synthesis (1994), (7), 669-71
 CODEN: SYNTBF; ISSN: 0039-7881
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 121:134061

AB Title compound I is a very useful intermediate for the synthesis five- and
 six-membered hetero-condensed pyridazinones, e.g., thienopyridazinone II and
 pyridopyridazinone III, in high yields under generally mild and simple
 reaction conditions.

L43 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:435499 HCAPLUS Full-text
 DOCUMENT NUMBER: 121:35499
 TITLE: Synthesis and evaluation of some 4,5-disubstituted
 6-phenyl-3(2H)-pyridazinones as hypotensive agents

AUTHOR(S): **Dal Piaz, V.; Giovannoni, M. P.**
 ; Laguna, R.; Cano, E.
 CORPORATE SOURCE: Dip. Sci. Farm., Florence, 50121, Italy
 SOURCE: European Journal of Medicinal Chemistry (1994),
 29(3), 249-52
 CODEN: EJMCA5; ISSN: 0223-5234
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Synthesis of the title compds. I (X = amino, nitro, methylthio, etc.; R = H,
 alkyl) was described. I were tested for hypotensive activity in normotensive
 rats.

L43 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:213001 HCAPLUS Full-text
 DOCUMENT NUMBER: 118:213001
 TITLE: Diels-Alder reactions on 5-acetyl-2-methyl-4-nitro-6-phenylpyridazin-3(2H)-one: a new facet of the pyridazine system
 AUTHOR(S): **Dal Piaz, Vittorio; Giovannoni, Maria P.**; Ciciani, Giovanna; Giomi, Donatella; Nesi, Rodolfo
 CORPORATE SOURCE: Dip. Sci. Farm., Univ. Florence, Florence, I-50121, Italy
 SOURCE: Tetrahedron Letters (1993), 34(1), 161-2
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 118:213001
 AB The title nitro ketone I was shown to react with 2,3-dimethylbuta-1,3- diene and cyclohexa-1,3-diene affording a mixture of the phthalazones II (R = NO₂, R₁ = H; RR₁ = bond) and the pyridazinone III, resp., through [2+4] cycloaddn. processes.

L43 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:656096 HCAPLUS Full-text
 DOCUMENT NUMBER: 115:256096
 TITLE: Isoxazolo[3,4-d]pyridazin-7(6H)-ones. Synthesis of 3-unsubstituted derivatives: a reinvestigation
 AUTHOR(S): **Dal Piaz, V.**; Ciciani, G.; **Giovannoni, M. P.**
 CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy
 SOURCE: Tetrahedron Letters (1991), 32(27), 3229-30
 CODEN: TELEAY; ISSN: 0040-4039
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Isoxazole I (R = CO₂Et, R₁ = CPh, R₂ = H) condensed with MeNHNH₂ or MeNHNH₂/polyphosphoric acid to give I (RR₁ = CONMeN:CH, R₂ = Ph; RR₁ = CONMeN:CPh, R₂ = H; resp.), which underwent catalytic hydrogenation to give pyridazinones II (R₃ = H, R₄ = CPh; R₃ = Ph, R₄ = CHO, resp.).

L43 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:583222 HCAPLUS Full-text
 DOCUMENT NUMBER: 115:183222
 TITLE: Reductive cleavage of isoxazolo[3,4-d]pyridazinones: a synthetic approach to various 4,5-functionalized 3(2H)-pyridazinones
 AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**
 CORPORATE SOURCE: Dip. Sci. Farm., Univ. Florence, Florence, 50121, Italy
 SOURCE: Heterocycles (1991), 32(6), 1173-9
 CODEN: HTCYAM; ISSN: 0385-5414
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 115:183222
 AB 4-Aminopyridazinones I (R = H, Me, Ph; R₁ = H, Me) were obtained in good yields by reductive ring opening of the isoxazole ring of isoxazolo[3,4-d]pyridazinones II. Starting from Et 4-acylisoxazole-3-carboxylates III (R₁ = H, Me), several pyridazinones IV (R = H, Me, Ph) are obtained in one step by treatment with RNHNH₂ and Pd/C.

L43 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:6499 HCAPLUS Full-text

DOCUMENT NUMBER: 116:6499

TITLE: Synthesis and evaluation of in vitro antitumor activity of some substituted 5-pyridazinyl-styrylketones

AUTHOR(S): Ciciani, Giovanna; **Dal Piaz, Vittorio; Giovannoni, Maria Paola**

CORPORATE SOURCE: Fac. Farm., Univ. Florence, Florence, 50121, Italy

SOURCE: Farmaco (1991), 46(7-8), 873-85

CODEN: FRMCE8; ISSN: 0014-827X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Isoxazolopyridazinone I (R = R1 = H) reacted with 4-R2C6H4CHO (R2 = H, OMe, Cl, F) to give I (RR1 = CHC6H4R2-4) (II). Treatment of acetylnitrophenylpyridazinone III (R = R1 = H, R3 = NO2) with amines (morpholine, pyrrolidine, piperidine, diethylamine, 2-methylaziridine) gave III [R3 = 4-morpholinyl, 1-pyrrolidinyl, 1-piperidinyl, diethylamino, 1-(2-methylaziridinyl)] which react with 4-R2C6H4CHO to give III (RR1 = CHC6H4R2-4) (IV). The antitumor activity of II and IV were measured against 60 human tumor cell lines.

L43 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:178836 HCAPLUS Full-text

DOCUMENT NUMBER: 112:178836

TITLE: New synthetic approach to pyrazolo[3,4-d]pyridazin-7(6H)-one ring system

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; **Giovannoni, Maria Paola**; Turco, Giovanni

CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121, Italy

SOURCE: Heterocycles (1989), 29(8), 1595-600

CODEN: HTCYAM; ISSN: 0385-5414

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 112:178836

AB Treatment of 2,6-disubstituted 5-acetyl-4-nitropyridazin-3(2H)-ones I (R = Me, Ph) with hydrazine or substituted hydrazines in alc. medium gives rise in high yields to new 1H- and 2H-pyrazolo[3,4-d]pyridizin-7(6H)-ones II and III (R1 = H, Me).

L43 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:477947 HCAPLUS Full-text

DOCUMENT NUMBER: 111:77947

TITLE: Oxidative cleavage of 7-oxo-6,7-dihydroisoxazolo[3,4-d]pyridazines by cerium(IV) diammonium nitrate. A synthetic approach to new 5-acyl-4-nitro-3-oxo-2,3-dihydropyridazines

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Turco, Giovanni

CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy

SOURCE: Synthesis (1989), (3), 213-14

CODEN: SYNTBF; ISSN: 0039-7881

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 111:77947

AB Treatment of oxodihydroisoxazolopyridazines I (R = Me, Ph, cyclohexyl; R1 = Me, Ph; R2 = Me, Et) with Ce(NH4)2(NO3)6 in an AcOH-H2O mixture containing HNO3 gave 30-53% acylnitrooxodihydropyridazines II (same R-R2).

L43 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:213879 HCAPLUS Full-text

DOCUMENT NUMBER: 106:213879

TITLE: Pyrazolo[1',5':1,6]pyrimido[4,5-d]pyridazin-7(8H)-one: a new heterocyclic ring system from isoxazolopyridazinones

AUTHOR(S): **Dal Piaz, Vittorio**; Ciciani, Giovanna; Chimichi, Stefano

CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, I-50121, Italy

SOURCE: Heterocycles (1986), 24(11), 3143-8
CODEN: HTCYAM; ISSN: 0385-5414

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 106:213879

AB Treatment of isoxazolopyridazinones I (R = H, Me; R1 = Me, Ph; R2 = Ph, 4-ClC6H4) with N2H4 afforded the pyrazole derivs. II which were converted in high yields into the new pyrazolopyrimidopyridazinones III by ring-closure with Ac2O.

L43 ANSWER 28 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1

ACCESSION NUMBER: 2006401269 EMBASE Full-text

TITLE: Novel pyrazolopyrimidopyridazinones with potent and selective phosphodiesterase 5 (PDE5) inhibitory activity as potential agents for treatment of erectile dysfunction.

AUTHOR: **Giovannoni M.P.; Vergelli C.**;
Biancalani C.; Cesari N.; Graziano A.; Biagini P.;
Gracia J.; Gavalda A.; **Dal Piaz V.**

CORPORATE SOURCE: M.P. Giovannoni, Dipartimento di Scienze Farmaceutiche,
Universita di Firenze, Via Ugo Schiff 6, Sesto
Fiorentino, 50019 Firenze, Italy.
mariapaola.giovannoni@unifi.it

SOURCE: Journal of Medicinal Chemistry, (24 Aug 2006) Vol. 49,
No. 17, pp. 5363-5371. .
Refs: 44

ISSN: 0022-2623 CODEN: JMCMAR

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 028 Urology and Nephrology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 14 Sep 2006

Last Updated on STN: 14 Sep 2006

AB Pyrazolo[1',5':1,6]pyrimido[4,5-d]**pyridazin**-4(3H)-ones and their analogues, potentially useful for the treatment of erectile dysfunction, were synthesized and evaluated as **inhibitors** of phosphodiesterase 5 (PDE5). Several compounds showed IC(50) values in the low nanomolar range, and in particular, compound 5r, displaying high potency toward PDE5 (IC(50) = 8.3 nM) and high selectivity versus PDE6 (240-fold) appeared to be a very promising new lead both in comparison with the potent but not selective sildenafil and in comparison with

some analogues previously reported by us. SAR studies in this triheterocyclic scaffold led us to conclude that the best arranged groups are a methyl in position 1, a benzyl in position 3, a phenyl in position 9, and a linear four-carbon chain in position 6. .COPYRG. 2006 American Chemical Society.

L43 ANSWER 29 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 2

ACCESSION NUMBER: 2006312087 EMBASE Full-text
 TITLE: Local anti-inflammatory effect and behavioral studies on new PDE4 **inhibitors**.
 AUTHOR: Pieretti S.; Dominici L.; Di Giannuario A.; Cesari N.; **Dal Piaz V.**
 CORPORATE SOURCE: S. Pieretti, Department of Drug Research and Evaluation, Italian National Institute of Health, Rome, Italy. pieretti@iss.it
 SOURCE: Life Sciences, (17 Jul 2006) Vol. 79, No. 8, pp. 791-800. .
 Refs: 45
 ISSN: 0024-3205 CODEN: LIFSAK
 PUBLISHER IDENT.: S 0024-3205(06)00188-3
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 052 Toxicology
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 1 Aug 2006
 Last Updated on STN: 1 Aug 2006

AB Phosphodiesterase 4 (PDE4) **inhibitors** are effective anti-inflammatory drugs, although some adverse effects are observed in animals and humans. These effects have forced researchers to find new PDE4 **inhibitors** with less adverse effects. We recently reported the synthesis of novel heterocyclic-fused **pyridazinones** that inhibit PDE4. As a first step in the study of the anti-inflammatory properties of these compounds, we studied the effects of local administration of these **pyridazinone** derivatives in a mouse model of acute inflammation. We found that 6-Benzyl-3-methyl-4-phenylpyrazolo[3,4-d]**pyridazin-7(6H)-one** (CC4), ethyl 6,7-dihydro-6-ethyl-3-methyl-7-oxo-4-phenyl-thieno[2,3-d] **pyridazine-2-carboxylate** (CC6) and ethyl 6,7-dihydro-6-ethyl-3- methyl-4-phenyl-1H-pyrrolo[2,3-d]**pyridazine-2-carboxylate** (CC12) reduced the paw edema induced by zymosan in mice as rolipram (the PDE4 inhibitor prototype with anti-inflammatory activity) and indomethacin did. It is well known that rolipram locally administered induces some adverse effects such as hyperalgesia. Thus, we studied this effect after local administration of CC4, CC6 and CC12 in the formalin test. We found that CC6 induced hyperalgesic effects, whereas CC4 and CC12 did not change the nociceptive threshold. Furthermore, we found that rolipram and CC6 reduced locomotor activity, whereas CC4 and CC12 did not change locomotor performance of the mice. Since CC4 and CC12 neither affected the nociceptive threshold nor changed the locomotor performance of mice, they appear more suitable than CC6 for future studies on animals and could be developed as an anti-inflammatory drug for humans. .COPYRG. 2006 Elsevier Inc. All rights reserved.

L43 ANSWER 30 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3

ACCESSION NUMBER: 2005174396 EMBASE Full-text
 TITLE: New pyrazolo[1',5':1,6]pyrimido[4,5-d]**pyridazin**

-4(3H)-ones as potent and selective PDE5
inhibitors.

AUTHOR: Feixas J.; **Giovannoni M.P.**; **Vergelli C.**; Gavalda A.; Cesari N.; Graziano A.; **Dal Piaz V.**

CORPORATE SOURCE: V. Dal Piaz, Dipto. di Scienze Farmaceutiche, Università di Firenze, Via U. Schiff 6, Sesto Fiorentino 50019, Firenze, Italy.
vittorio.dalpiaz@unifi.it

SOURCE: Bioorganic and Medicinal Chemistry Letters, (2 May 2005) Vol. 15, No. 9, pp. 2381-2384. .
Refs: 27
ISSN: 0960-894X CODEN: BMCLE8

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 26 May 2005
Last Updated on STN: 26 May 2005

AB A series of potent PDE5 **inhibitors** with high selectivity versus PDE6 isoenzymes was identified. .COPYRGT. 2005 Elsevier Ltd. All rights reserved.

L43 ANSWER 31 OF 38 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 4

ACCESSION NUMBER: 2003113289 EMBASE Full-text

TITLE: Novel 3-arylamino- and 3-cycloalkylamino-5,6-diphenyl-**pyridazines** active as ACAT **inhibitors**

AUTHOR: Toma L.; **Giovannoni M.P.**; **Vergelli C.**; **Dal Piaz V.**; Kwon B.-M.; Kim Y.-K.; Gelain A.; Barlocco D.

CORPORATE SOURCE: L. Toma, Dipartimento di Chimica Organica, Università di Pavia, Via Taramelli 10, 27100 Pavia, Italy.
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SOURCE: Archiv der Pharmazie, (2002) Vol. 335, No. 11-12, pp. 563-566. .
Refs: 13
ISSN: 0365-6233 CODEN: ARPMAS

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 27 Mar 2003
Last Updated on STN: 27 Mar 2003

AB A new series of **pyridazine** derivatives, structurally related to the previously reported ACAT **inhibitors** 3-(cyclo)alkylamino-5,6-diphenyl-**pyridazines**, were synthesized and tested for their inhibitory properties. Substitution of the 3-alkylamino chain with a phenylamino group maintains activity. In contrast, the presence of either substituents on the phenylamino group or aliphatic rings having more or less than six carbon atoms lowers it.

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DUPLICATE 9

ACCESSION NUMBER: 97142951 EMBASE Full-text
 DOCUMENT NUMBER: 1997142951
 TITLE: Novel heterocyclic-fused **pyridazinones** as potent and selective phosphodiesterase IV **inhibitors**.
 AUTHOR: Piaz V.D.; **Giovannoni M.P.**; Castellana C.; Palacios J.M.; Beleta J.; Domenech T.; Segarra V.
 CORPORATE SOURCE: V.D. Piaz, Dipto. di Scienze Farmaceutiche, via Gino Capponi 9, 50121 Firenze, Italy
 SOURCE: Journal of Medicinal Chemistry, (1997) Vol. 40, No. 10, pp. 1417-1421. .
 Refs: 31
 ISSN: 0022-2623 CODEN: JMCMAR
 COUNTRY: United States
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 030 Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 4 Jun 1997
 Last Updated on STN: 4 Jun 1997

AB A series of 6-aryl-4,5-heterocyclic-fused **pyridazinones** were designed and synthesized as selective phosphodiesterase (PDE) IV **inhibitors**. Biological evaluation of these compounds demonstrated a good selectivity profile toward the PDE IV family and greatly attenuated affinity for the Rolipram high-affinity binding site that seems to be responsible for undesirable side effects. Structure-activity relationships (SARs) studies showed that the presence of an ethyl group at **pyridazine** N-2 is associated with the best potency and selectivity profile.

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ACCESSION NUMBER: 2002129062 EMBASE Full-text
 TITLE: Airway relaxant and anti-inflammatory properties of a PDE4 inhibitor with low affinity for the high-affinity rolipram binding site.
 AUTHOR: Martin C.; Goggel R.; **Dal Piaz V.**; **Vergelli C.**; **Giovannoni M.P.**; Ernst M.; Uhlig S.
 CORPORATE SOURCE: S. Uhlig, Division of Pulmonary Pharmacology, Research Centre Borstel, Parkallee 22, 23845 Borstel, Germany. suhlig@fzborstel.de
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (2002) Vol. 365, No. 4, pp. 284-289. .
 Refs: 31
 ISSN: 0028-1298 CODEN: NSAPCC
 COUNTRY: Germany
 DOCUMENT TYPE: Journal; Article
 FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
 030 Pharmacology
 037 Drug Literature Index
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 ENTRY DATE: Entered STN: 18 Apr 2002
 Last Updated on STN: 18 Apr 2002
 AB **Inhibitors** of phosphodiesterase 4 (PDE4) possess bronchospasmolytic and anti-inflammatory properties, which make them very attractive drugs for the

treatment of asthma and COPD. Unfortunately, many PDE4 **inhibitors** also produce central nervous and gastrointestinal side effects, which have limited their clinical application. PDE4 has two binding sites for the archetypal PDE4 inhibitor rolipram, and it has been suggested that binding to the high-affinity rolipram binding site (HARBS) is responsible for the side effects of PDE4 **inhibitors**. Recently, we have synthesised the PDE4 inhibitor CC3 which shows low affinity to the HARBS. In the present study we investigated the bronchospasmolytic and anti-inflammatory properties of this novel compound in comparison to rolipram and the PDE3 inhibitor motapizone. The airway-relaxant properties of the PDE **inhibitors** were analysed in rat precision-cut lung slices (PCLS) in which airways were contracted by methacholine or in passively sensi-tised PCLS exposed to ovalbumin. The anti-inflammatory properties were investigated by measuring the release of TNF from endotoxin-treated human monocytes. Up to concentrations of 10µM none of the PDE **inhibitors** significantly affected bronchoconstriction elicited by 10µM methacholine. However, if rolipram or CC3 were given in combination with motapizone, methacholine-induced bronchoconstriction was concentration-dependently attenuated. Allergen-induced bronchoconstriction in passively sensitised PCLS was attenuated by CC3 (IC(50) 2.7 µM), rolipram (0.23µM) and motapizone (8µM). Combination of equimolar concentrations of motapizone and CC3 (0.34µM) or rolipram (0.005µM) showed an additive effect. Endotoxin-induced TNF release from human monocytes was attenuated by all three PDE **inhibitors**, i.e. CC3 (IC(50) 4.6 µM), rolipram (0.18 µM) and motapizone (5.8µM). Our findings suggest that PDE4 **inhibitors** with only low affinity for the HARBS have bronchospas-molytic and anti-inflammatory properties.

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ACCESSION NUMBER: 97024236 EMBASE Full-text

DOCUMENT NUMBER: 1997024236

TITLE: Synthesis and evaluation as PDE IV **inhibitors** of 4,5-hetero-condensed-6-phenyl-3(2H)-**pyridazinones**.

AUTHOR: Dal Piaz V.; Giovannoni M.P.; Castellana C.; Palacios J.M.; Beleta J.; Domenech T.; Segarra V.

CORPORATE SOURCE: V. Dal Piaz, Dipto. di Scienze Farmaceutiche, Via Gino Capponi 9, 50121 Firenze, Italy

SOURCE: Acta Pharmaceutica Hungarica, (1996) Vol. 66, No. SUPPL., pp. S33-S34. . Refs: 9

COUNTRY: Hungary ISSN: 0001-6659 CODEN: APHGAO

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: English

ENTRY DATE: Entered STN: 14 Feb 1997

Last Updated on STN: 14 Feb 1997

L43 ANSWER 35 OF 38 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:412197 BIOSIS Full-text

DOCUMENT NUMBER: PREV200200412197

TITLE: 1,2,4-triazolo(4,3-b)pyrido(3,2-d)**pyridazine** derivatives and pharmaceutical compositions containing them.

AUTHOR(S): **Gracia Ferrer, Jordi** [Inventor, Reprint author]; Crespo Crespo, Ma Isabel [Inventor]; Vega

Noverola, Armando [Inventor]; Fernandez Garcia, Andres [Inventor]
 CORPORATE SOURCE: Barcelona, Spain
 ASSIGNEE: Almirall Prodesfarma, S.A., Barcelona, Spain
 PATENT INFORMATION: US 6407108 20020618
 SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 18, 2002) Vol. 1259, No. 3. <http://www.uspto.gov/web/menu/patdata.html>. e-file.
 CODEN: OGUPE7. ISSN: 0098-1133.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 ENTRY DATE: Entered STN: 31 Jul 2002
 Last Updated on STN: 31 Jul 2002
 AB Heterocyclic compounds of formula(I), ##STR1## wherein R1 represents a hydrogen atom or a --(CH2)m --Y group, wherein m is an integer from 0 to 4 and Y represents an alkyl, haloalkyl, alkoxy, alkoxy carbonyl, C3 -C7 cycloalkyl, norbornyl or phenylalkenyl group, or an aromatic group which aromatic group may optionally be substituted by one or more halogen atoms; R2 represents an aromatic group which aromatic group may optionally be substituted by one or more halogen atoms or alkyl, alkoxy, C3 -C6 cycloalkoxy, methylenedioxy, nitro, dialkylamino or trifluoromethyl groups, and R3 represents a hydrogen or halogen atom or an alkyl group, and pharmaceutically acceptable salts thereof, processes for preparing the same are disclosed herein. The compounds are phosphodiesterase 4 **inhibitors**.

L43 ANSWER 36 OF 38 MEDLINE on STN

ACCESSION NUMBER: 2001676035 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 11708931
 TITLE: 5,6-Diphenylpyridazine derivatives as acyl-CoA:cholesterol acyltransferase **inhibitors**

AUTHOR: **Giovannoni M P**; Piazz V D; Kwon B M; Kim M K; Kim Y K; Toma L; Barlocco D; Bernini F; Canavesi M
 CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Firenze, via G. Capponi 9, 50121 Firenze, Italy.. mariapaola.giovannoni@unifi.it
 SOURCE: Journal of medicinal chemistry, (2001 Nov 22) Vol. 44, No. 24, pp. 4292-5.
 Journal code: 9716531. ISSN: 0022-2623.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200112
 ENTRY DATE: Entered STN: 28 Nov 2001
 Last Updated on STN: 23 Jan 2002
 Entered Medline: 12 Dec 2001

AB Alkyl-5,6-diphenylpyridazine derivatives combining several main features of ACAT **inhibitors**, such as a long alkyl side chain linked to a heterocycle and the o-diphenyl system, were synthesized and tested. Moreover, modeling studies on representative terms were performed. Some compounds displayed ACAT inhibition in the micromolar range, both on the enzyme isolated from rat liver microsomes and in cell-free homogenate of murine macrophages.

L43 ANSWER 37 OF 38 MEDLINE on STN

ACCESSION NUMBER: 1998032732 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 9366028

TITLE: Chiral resolution and absolute configuration of the enantiomers of 5-acetyl-2-methyl-4-methylsulfinyl-6-phenyl-3(2H)-**pyridazinone** and evaluation of their platelet aggregation inhibitory activity.

AUTHOR: Azzolina O; **Dal Piaz V**; Collina S; **Giovannoni M P**; Tadini C

CORPORATE SOURCE: Dipartimento di Chimica Farmaceutica, Universita di Pavia, Italy.

SOURCE: Chirality, (1997) Vol. 9, No. 7, pp. 681-5.
Journal code: 8914261. ISSN: 0899-0042.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199801

ENTRY DATE: Entered STN: 29 Jan 1998
Last Updated on STN: 29 Jan 1998
Entered Medline: 12 Jan 1998

AB In a series of 5-acyl-6-phenyl-2,4-substituted-3(2H)-pyridazines the derivative 1a, with a sulfur stereogenic center, had the most potent activity as human platelet aggregation inhibitor. The resolution of rac-1a was successfully performed by chiral chromatography on Chiralcel OD-R, OD-H, and Chiralpak AD columns and scaled up to a preparative level. The absolute configuration of (-)-(S)-1a was determined by X-ray crystallographic analysis. In vitro human platelet aggregation inhibitory activity was evaluated. Both the enantiomers showed IC50 values in the same micromolar range, but the (-)-(S) isomer was slightly more potent [(S)/(R) potency ratio was 4/1].

L43 ANSWER 38 OF 38 MEDLINE on STN

ACCESSION NUMBER: 97453368 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 9299216

TITLE: Study of the antisecretory and antiulcer mechanisms of a new indenopyridazinone derivative in rats.

AUTHOR: Barocelli E; Chiavarini M; Ballabeni V; Barlocco D; Vianello P; **Dal Piaz V**; Impicciatore M

CORPORATE SOURCE: Istituto di Farmacologia e Farmacognosia, Universita degli Studi di Parma, Italy.

SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, (1997 May) Vol. 35, No. 5, pp. 487-92.
Journal code: 8907422. ISSN: 1043-6618.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199711

ENTRY DATE: Entered STN: 24 Dec 1997
Last Updated on STN: 24 Dec 1997
Entered Medline: 24 Nov 1997

AB The present study investigates the antisecretory and antiulcer mechanisms of a new indenopyridazinone derivative previously reported to inhibit gastric acid secretion in pylorus-ligated rats and to prevent gastric ulcerations induced by indomethacin or ethanol in the same animal species. The new compound was tested on the acid hypersecretion induced by histamine, pentagastrin and bethanechol in in vivo and in vitro experimental models. Furthermore, its influence on the mucosal layer adhering the gastric wall in indomethacin-treated rats was considered. Ranitidine was selected as a reference drug. The results obtained demonstrated that the new molecule, at variance with ranitidine, exerts antiulcer activity mainly enhancing the gastric mucosal

integrity and simultaneously inhibiting the gastric acid hypersecretion evoked exclusively by cholinergic pulses. Therefore, an involvement of a neuronal rather than an effectorial mechanism has been suggested. Due to these mechanisms of action it clearly differentiates from ranitidine and its possible application in the peptic disease resistant to H₂-blockers could be speculated.

=> d his nofile

(FILE 'HOME' ENTERED AT 10:33:12 ON 15 DEC 2006)

FILE 'HCAPLUS' ENTERED AT 10:34:12 ON 15 DEC 2006

L1 1 SEA ABB=ON PLU=ON US20060173008/PN
D SCAN
SEL RN

FILE 'REGISTRY' ENTERED AT 10:34:38 ON 15 DEC 2006

L2 458 SEA ABB=ON PLU=ON (720718-30-9/BI OR 101601-80-3/BI OR
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OR 119830-47-6/BI OR 120-61-6/BI OR 126747-14-6/BI OR
13207-66-4/BI OR 134842-97-0/BI OR 137-07-5/BI OR 13922-41-
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L3 STR

L4 0 SEA SSS SAM L3

L5 STR L3

L6 0 SEA SSS SAM L5

D QUE STAT

L7 STR L5

L8 43 SEA SSS SAM L7

L9 STR L5

L10 43 SEA SSS SAM L9

L11 974 SEA SSS FUL L9

SAV L11 JAI821/A

L12 305 SEA ABB=ON PLU=ON L11 AND L2

FILE 'HCAPLUS' ENTERED AT 10:46:07 ON 15 DEC 2006

L13 5 SEA ABB=ON PLU=ON L12

D 5 IBIB ABS
 L14 37 SEA ABB=ON PLU=ON L11
 D SCAN L1
 L15 23 SEA ABB=ON PLU=ON L14 AND (THU OR BIOL OR BSU)/RL
 L16 30 SEA ABB=ON PLU=ON L14 AND (1840-2003)/PRY,AY,PY
 L17 34 SEA ABB=ON PLU=ON L15 OR L16
 D L1 IBIB
 L18 77 SEA ABB=ON PLU=ON DAL PIAZ, V?/AU
 L19 4 SEA ABB=ON PLU=ON AGUILAR IZQUIERDO, N?/AU
 L20 9 SEA ABB=ON PLU=ON BUIL ALBERO MARIA, A?/AU
 L21 2 SEA ABB=ON PLU=ON CARRASCAL RIERA, M?/AU
 L22 10 SEA ABB=ON PLU=ON GRACIA FERRER, J?/AU
 L23 41 SEA ABB=ON PLU=ON GIOVANNONI, M?/AU
 L24 15 SEA ABB=ON PLU=ON VERGELLI, C?/AU
 L25 27 SEA ABB=ON PLU=ON L14 AND ((L18 OR L19 OR L20 OR L21 OR
 L22 OR L23 OR L24))
 L26 5 SEA ABB=ON PLU=ON L16 NOT L25
 SEL HIT RN 1-

FILE 'MARPAT' ENTERED AT 10:53:21 ON 15 DEC 2006

L27 6 SEA SSS SAM L9
 L28 102 SEA SSS FUL L9

FILE 'REGISTRY' ENTERED AT 10:53:59 ON 15 DEC 2006

L29 0 SEA ABB=ON PLU=ON L11 AND MEDLINE/LC
 L30 0 SEA ABB=ON PLU=ON L11 AND BIOSIS/LC
 L31 0 SEA ABB=ON PLU=ON L11 AND EMBASE/LC

FILE 'EMBASE, BIOSIS, MEDLINE' ENTERED AT 10:54:47 ON 15 DEC 2006

L32 0 SEA ABB=ON PLU=ON AGUILAR IZQUIERDO, N?/AU
 L33 2 SEA ABB=ON PLU=ON BUIL ALBERO MARIA, A?/AU
 L34 0 SEA ABB=ON PLU=ON CARRASCAL RIERA, M?/AU
 L35 2 SEA ABB=ON PLU=ON GRACIA FERRER, J?/AU
 L36 113 SEA ABB=ON PLU=ON GIOVANNONI, M?/AU
 L37 26 SEA ABB=ON PLU=ON VERGELLI, C?/AU
 L38 35 SEA ABB=ON PLU=ON (L32 OR L33 OR L34 OR L35 OR L36 OR
 L37) AND (PYRIDAZIN? AND INHIBITORS?)
 D IBIB
 L39 117 SEA ABB=ON PLU=ON DAL PIAZ, V?/AU
 L40 35 SEA ABB=ON PLU=ON L39 AND (PYRIDAZIN? AND INHIBITORS?)
 L41 39 SEA ABB=ON PLU=ON L38 OR L40

FILE 'HCAPLUS' ENTERED AT 11:16:50 ON 15 DEC 2006

D L26 4-5 IBIB FHITSTR
 SEL L26 HIT RN 1-
 D QUE L16
 L42 5 SEA ABB=ON PLU=ON L16 NOT L25
 D L42 1-5 IBIB ED AB HITSTR HITIND
 D QUE L25
 E QUE L34
 D QUE L41

FILE 'HCAPLUS, EMBASE, BIOSIS, MEDLINE' ENTERED AT 11:19:51 ON 15 DEC 2006

L43 38 DUP REM L25 L41 (28 DUPLICATES REMOVED)
 ANSWERS '1-27' FROM FILE HCAPLUS
 ANSWERS '28-34' FROM FILE EMBASE
 ANSWER '35' FROM FILE BIOSIS
 ANSWERS '36-38' FROM FILE MEDLINE
 D L43 1-38 IBIB AB